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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,157	08/16/2001	Hiroo Imura	299002032411	2951

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EXAMINER	
NICHOLS, CHRISTOPHER J	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/931,157	IMURA ET AL.	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-39* is/are pending in the application.

4a) Of the above claim(s) *22-34,38 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *22-39* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/121,446.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5 August 2003 has been entered.

2. Claims **1-22** have been cancelled. Claims **23-34** and **38-39** remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Claims **35-37** are under examination.

3. All previously made Rejections of claims **35-37** are hereby *withdrawn* in view of Applicant's amendments to said claims (5 August 2003). This does not in any way reflect on the validity of the previous rejections. It is done because Applicant has changed SEQ ID NO and disease state targeted in the claims as instantly presented thus warranting a new rejection to properly and fully address the new limitations introduced in the Amendment filed (5 August 2003).

Sequence Rules

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the

reason(s) set forth below. This application discloses a nucleic acid and amino acid sequences in Figures 1 and 2 without the appropriate SEQ ID NO's. Correction is required.

Specification

5. The amendment filed 25 September 2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment filed 25 September 2002 inserts unsupported material which describes a screening assay to identify agonists and/or antagonists that have an affinity for SEQ ID NO: 1. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims **35-37** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

invention. The newly amended claims are wholly drawn to support garnered from the Amendment filed 25 September 2002 which constitutes, in and of itself, new matter (see Objection above). While it is understood that Applicant is not required to have literal support for the claims, the Applicant as filed focuses on the isolation and characterization of a novel endothelin receptor. Therefore the support for a screening, characterizing, and therapeutic methods in the amendment is inconsistent with the spirit of the application as filed. Therefore the claims as currently presented have no support in the application as originally filed.

7. Claims **35-37** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

8. The claims are drawn broadly to a method of first screening, the characterizing, and the utilizing the compound so identified as a therapeutic agent for an as of yet unspecified circulatory system disease. The language of said claims encompasses screening assay, characterization, and therapy.

9. The specification teaches that SEQ ID NO: 2 encodes SEQ ID NO: 1, a novel endothelin receptor.

10. The specification as filed does not provide any guidance or examples that would enable a skilled artisan to use the disclosed methods of screening, characterizing, and using an as of yet undisclosed compound to treat a circulatory system disease a patient. Therefore the claims as currently presented represent an invitation to experiment.

11. The specification fails to provide any guidance for the successful treatment or alleviation of symptoms of any circulatory system disease, and since resolution of the various complications in regards to screening, characterizing, and successfully using a compound to treat circulatory system diseases is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed *in vivo* would require the *de novo* isolation, characterization, and then evaluation of the efficacy of the unknown compound related proteins, signs, and symptoms to correlate with successful treatment of a circulatory system disease. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed. Further since the claims as written comprising three discrete steps: isolation, characterization, and use as a therapeutic, the skilled artisan is confronted with three steps with no predictability and no guidance.

12. Additionally, a person skilled in the art would recognize that predicting the efficacy of using an as of yet unidentified or characterized compound *in vivo* based solely on prophetic guidance of its existence and properties as highly problematic (see MPEP §2164.02). Thus, although the specification prophetically considers and discloses general methodologies of using the claimed methods to isolate, characterize, and use in therapeutic methods for a circulatory system disease, such a disclosure would not be considered enabling since the state of circulatory system diseases is highly unpredictable. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

13. The following references are cited herein to illustrate the state of the art of circulatory system diseases and endothelin receptors.

14. Regarding the breadth of the claims, the art recognizes that "agent" can pertain to chemical entities, pharmaceutical compositions, proteins, peptides, non-peptide compounds, animal tissue extracts, vegetable extracts, cell extracts, synthetic agents, biologically derived substances as well as proteinaceous substances, known, and unknown compounds. Thus the claims as written constitute an invitation to experiment with any given agent of any nature and structure so that only through undue and unpredictable experimentation may the skilled artisan identify a compound which potentially has the desired activity.

15. On the nature of the invention, US 5,837,241 (17 November 1998) Ferrara *et al.* and US 6,545,048 B1 (8 April 2003) Patterson & Lahav teach that endothelin antagonists and/or inhibitors can be used in therapies for heart failure and cancer, respectively. Thus even if the skilled artisan were able to practice the invention to identify a candidate compound which binds to the endothelin receptor the skilled artisan must then move onto characterizing it for its therapeutic value. And, in light of the references above, even if therapeutic it is not predictable to be for a circulatory system disease *per se.* This is further supported by US 6,147.051 (14

November 2000) Watanabe *et al.* who teaches that compounds having antagonistic activity on endothelin receptors are suggested to be effective as therapeutic drugs for hypertension, cardiac or cerebral circulatory disease, renal disease, and asthma (Col. 1 lines 30-44). While compounds which bind the endothelin receptor may constitute a fecund area of investigation, the CAFC held in *Genentech Inc. v. Novo Nordisk A/S* (CA FC) **42 USPQ2d 1001** (1997) that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Citing *Brenner v. Manson,* **383 U.S. 519, 536, 148 USPQ 689, 696** (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore the CFAC stated that tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in the instant specification with respect to any compound that binds SEQ ID NO: 1 (an endothelin receptor) which in turns has therapeutic activity for any given circulatory system disease.

16. On the level of predictability in the art, Wenzel *et al.* (May 1994) "Endothelin Receptor Antagonists Inhibit Endothelin in Human Skin Microcirculation." Hypertension **23**(5): 581-586 teaches that the role of endothelin (the natural ligand of the endothelin receptors) in physiology and disease is unclear. The administration of endothelin leads to transient vasodilatation followed by long-lasting and profound vasoconstriction. The role of endothelin in humans is unknown and the role of endothelin in arterial hypertension is controversial. Thus the skilled

artisan is confronted with first identify, then characterizing the activity of, and therapeutic value of a class of compounds wherein the natural analog's activity is unknown and role in circulatory system disease such as hypertension is not predictable.

17. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from prophetic guidance and suggestion to the *in vivo* therapy of any given circulatory system disease as exemplified in the references herein. Consequently, it would require undue experimentation for the artisan to practice the invention.

18. Claims **35-37** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

19. The claims require that the compound which is administered to the subject to accomplish the preamble of "treating a circulatory system disease" must first be identified by screening a library of compounds and then confirmed via a binding assay therefore the compound used is not known or must be confirmed. This constitutes an invitation to experiment and demonstrates that Applicant did not actually possess said compound at the time of filing the instant application as the art recognizes that "compound" can pertain to chemical entities, pharmaceutical compositions, proteins, peptides, non-peptide compounds, animal tissue extracts, vegetable extracts, cell extracts, synthetic agents, biologically derived substances as well as proteinaceous substances, known, and unknown compounds.

20. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is disclosed is method for discovering and characterizing the compound. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

21. To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

22. See *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003). In *University of Rochester v. G.D. Searle & Co.* a patent directed to method for inhibiting prostaglandin synthesis in human host using unspecified compound, in order to relieve pain without side effect of stomach irritation, did not satisfy written description requirement of 35 U.S.C. §112, since patent described the compound's desired function of reducing activity of enzyme PGHS-2 without adversely affecting PGHS-1 enzyme activity, but did not identify said compound, since invention consists of performing "assays" to screen compounds in order to discover those with desired effect, but patent did not name even one compound that assays would identify as suitable for practice of invention, or provide information such that one skilled in art could identify suitable compound, since specification did not indicate that compounds are available in public depository, since claimed treatment method cannot be practiced without compound, and since inventors thus cannot be said to have "possessed" claimed invention without knowing of compound or method certain to produce compound. Thus said patent constituted an invitation to experiment to first identify, then characterize, and the use a therapeutic a class of compounds defined only by their desired properties.

23. Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

24. Claim **35** and **36** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Both claims recite the limitation of an amino acid sequence of SEQ ID NO: 1 but SEQ ID NO: 1 is a nucleic acid sequence. Therefore said claims are indefinite.

Summary

25. Claims **35-37** are hereby rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 571-272-0889. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 571-272-0887. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary L. Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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CJN
January 26, 2004